



4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2013-D-0369]

International Conference on Harmonisation; Draft Guidance on M7 Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance entitled “M7 Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk.” The draft guidance was prepared under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The draft guidance emphasizes considerations of both safety and quality risk management in establishing levels of mutagenic impurities that are expected to pose negligible carcinogenic risk. It outlines recommendations for assessment and control of mutagenic impurities that reside or are reasonably expected to reside in a final drug substance or product, taking into consideration the intended conditions of human use. The draft guidance is intended to provide guidance for new drug substances and new drug products during their clinical development and subsequent applications for marketing.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115 (g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft

guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE  
FEDERAL REGISTER].

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993-0002, or the Office of Communication, Outreach and Development (HFM-40), Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852-1448. Send one self-addressed adhesive label to assist the office in processing your requests. The draft guidance may also be obtained by mail by calling CBER at 1-800-835-4709 or 301-827-1800. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to <http://www.regulations.gov>.

Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT:

Regarding the guidance:

David Jacobson-Kram,  
Office of New Drugs,  
Center for Drug Evaluation and Research,  
Food and Drug Administration,  
10903 New Hampshire Ave.,  
Bldg. 32, rm. 5299,  
Silver Spring, MD 20993-0002,

301-796-0175.

Regarding the ICH:

Michelle Limoli,  
International Programs,  
Center for Drug Evaluation and Research,  
Food and Drug Administration,  
10903 New Hampshire Ave.,  
Bldg. 51, rm. 3342,  
Silver Spring, MD 20993-0002,  
301-796-8377.

SUPPLEMENTARY INFORMATION:

I. Background

In recent years, many important initiatives have been undertaken by regulatory authorities and industry associations to promote international harmonization of regulatory requirements. FDA has participated in many meetings designed to enhance harmonization and is committed to seeking scientifically based harmonized technical procedures for pharmaceutical development. One of the goals of harmonization is to identify and then reduce differences in technical requirements for drug development among regulatory agencies.

ICH was organized to provide an opportunity for tripartite harmonization initiatives to be developed with input from both regulatory and industry representatives. FDA also seeks input from consumer representatives and others. ICH is concerned with harmonization of technical requirements for the registration of pharmaceutical products among three regions: The European Union, Japan, and the United States. The six ICH sponsors are the European Commission; the

European Federation of Pharmaceutical Industries Associations; the Japanese Ministry of Health, Labour, and Welfare; the Japanese Pharmaceutical Manufacturers Association; the Centers for Drug Evaluation and Research and Biologics Evaluation and Research, FDA; and the Pharmaceutical Research and Manufacturers of America. The ICH Secretariat, which coordinates the preparation of documentation, is provided by the International Federation of Pharmaceutical Manufacturers Associations (IFPMA).

The ICH Steering Committee includes representatives from each of the ICH sponsors and the IFPMA, as well as observers from the World Health Organization, Health Canada, and the European Free Trade Area.

In February 2013, the ICH Steering Committee agreed that a draft guidance entitled “M7 Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk” should be made available for public comment. The draft guidance is the product of the M7 Expert Working Group of the ICH. Comments about this draft will be considered by FDA and the M7 Expert Working Group.

The draft guidance provides guidance on the regulation of genotoxic impurities in new drug substances and drug products.

This draft guidance is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the Agency’s current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

## II. Comments

Interested persons may submit either electronic comments regarding this document to <http://www.regulations.gov> or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at <http://www.regulations.gov>.

### III. Electronic Access

Persons with access to the Internet may obtain the document at <http://www.regulations.gov>,  
<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>,  
or  
<http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

Dated: April 9, 2013.

Leslie Kux,

Assistant Commissioner for Policy.